

Double Blind Study of Bisoprolol and Atenolol in Hypertension and Myocardial Infarction in Human Subjects

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Abstract:

Objectives: To compare the efficacy of bisoprolol and atenolol in hypertension, myocardial infarction and effect on lipid levels.

Materials and methods:

18 patients whose blood pressure was above 95mm Hg (Diastolic) or higher were recruited from hypertension clinic. They were given either A or B alternatively. B.P. were recorded both supine and standing position at 30 minutes interval after 2 weeks again B.P. was recorded. In the same way 14 patients were recruited for myocardial infarction. Before giving the drug E.C.G. and blood for lipid profile were taken. After 4 weeks again the same procedure were repeated. Results were tabulated and comparison and significance were tested by unpaired students 't' test and their 'p' value was calculated. Results were also shown graphically.

Results

Bisoprolol had consistently significant effect than atenolol in hypertension, myocardial infarction and in reducing lipid profile levels.

Summary and conclusion:

In this double blind study, bisoprolol had consistently greater antihypertensive effect than atenolol ($p < 0.05 > 0.02$) in supine and in standing ($p < 0.01 > 0.001$). In Myocardial infarction, bisoprolol worked more quickly than atenolol. Bisoprolol statistically significant in reducing blood triglycerides and LDL levels. So the efficacy of Bisoprolol is more both in hypertension and in myocardial infarction.

Key words: Atenolol, bisoprolol, hypertension, Myocardial infarction

I. Introduction

Hypertension and myocardial infarction are probably the most important public health problems today. The role of sympathetic nervous system in the etiology of hypertension has been well established. So alpha and beta adrenergic antagonists were tried since 1958. The cardio selective beta 1 blockers continue to be the 1st choice⁽¹⁾ The newer beta 1 blocker bisoprolol had got much more efficacy over atenolol. Many studies had done previously^(2,3) So, a double blind study was done on human subjects at Government General Hospital Guntur.

II. Aims And Objectives

To compare the efficacy of bisoprolol 5mg and atenolol 50mg in hypertension(3,14) and myocardial infarction⁽¹⁵⁻¹⁷⁾ and also for reducing the lipid profile levels in the body^(18,19)

III. Drugs

3.1 Bisoprolol²⁰⁻²⁵

It is a derivative of phenoxyamino propranolol. It is more lipophilic than atenolol so it had got more absorption rate. Plasma protein binding is 30. Plasma t_{1/2} 10-12 hrs. It is a well tolerated drug.

3.2 Atenolol

It is strongly hydrophilic and poorly lipophilic. Plasma protein binding is 5. Plasma t_{1/2} 68 hrs. Biological half life 20hrs. It is also well tolerated

IV. Materials And Methods

It was a double blind study performed at hypertension and cardiology of Government General Hospital, Guntur. After getting drug from companies the medicines were prepared by the clinical pharmacologist as in two

separate capsules and the code was given as drug A and drug B. Only after completion of the study it was decoded and that particular drug was informed to the investigator. Both male and female patients are included. Pediatric patients with history of congestive heart failure, renal failure, liver disease, pulmonary disease, hematological diseases, and pregnant ladies are excluded. 18 patients were recruited for hypertension for 2 weeks and given either drug A or drug B alternatively. BP was recorded in supine and standing positions at 30 min interval at the same time of the day. 14 patients were recruited for myocardial infarction for 4 weeks and given either drug A or drug B alternatively.

Before & after ECG and blood for lipid profile were taken. All results were tabulated and comparison and significance were tested by unpaired student t test and their P values were calculated. Results were shown graphically also.

V. Results

Bisoprolol had a consistently greater antihypertensive effect than Atenolol. Compared with Atenolol, Bisoprolol reduced mean supine blood pressure – 22.56 mm Hg (diastolic) and -47 mm Hg (Systolic). The corresponding reductions seen with Atenolol were -12.11 mm Hg and -33.33 mm Hg respectively. The difference in antihypertensive effect between Atenolol and Bisoprolol were statistically very significant for diastolic blood pressure ($p < 0.05 > 0.22$) in supine position. The difference between the two was not of much significance for systolic blood pressure ($p = 0.10$).

Similarly Bisoprolol achieved significantly greater reductions in standing blood pressure reducing the diastolic blood pressure by -20.33 mm Hg and systolic blood pressure -45.44 mm Hg corresponding figures for Atenolol were -8.56 mm Hg and -30.33 mm Hg respectively. The difference in antihypertensive effect between Atenolol and Bisoprolol was statistically very significant for diastolic ($p < 0.01 > 0.001$). The difference between the two was not of much significance for systolic blood pressure ($p > 0.55$).

5.1. In Myocardial Infarction

All patients except two responded well to both Bisoprolol and Atenolol. But Bisoprolol worked more quickly than Atenolol. It reduced the symptoms like chest pain from 2 hrs to 24 hrs. Atenolol reduced it from 6 hrs to 48 hrs. Both drugs reduced the mean resting heart rate, but the difference is not statistically significant ($p > 0.10$).

5.2 E.C.G. Findings

Both the drugs reduced the QTC values except in two patients. But the difference between these two drugs were not statistically significant ($p > 0.10$).

5.3 Lipid Profile Values:

Bisoprolol decreased the serum triglycerides, serum cholesterol, LDL and VLDL levels and it increased the cardio protective HDL levels.

On the whole Atenolol increased the Serum triglycerides, serum cholesterol, LDL and VLDL levels and it decreased the cardio protective HDL levels.

Bisoprolol significantly decreased the triglyceride level ($p < 0.01$) as well as LDL levels ($p < 0.05 > 0.01$). The difference between the two drugs in other parameters was not statistically significant.

5.4 Adverse effect in both hypertension and myocardial infarction:

The side effects noted in patients under Bisoprolol were tingling, numbness, tiredness, easy fatigability, muscular cramps, muscular weakness and head-ache. They were moderate in intensity and did not necessitate withdrawal from the trial.

The other symptoms noted in patients under Atenolol were tingling, fatigability, muscular cramps, muscular weakness and head-ache. They were also moderate in intensity and did not necessitate withdrawal from the trial. The side effects disappeared early with Bisoprolol than with Atenolol.

So, Bisoprolol did well both in hypertension and myocardial infarction when compared to Atenolol and also significantly decreased the triglycerides and LDL levels.

Changes in systolic and Diastolic blood pressure seen during treatment with Bisoprolol and Atenolol in patients with essential hypertension.

Table 1: Parameters:

Parameters	Under Bisoprolol		Under Atenolol		Mean Diff.	Standard Error	't' Value	'p' Value
	Mean	S.D.	Mean	S.D.				
Supine Systolic Blood Pressure	-47.00	+19.69	-33.33	+12.85	13.67	7.84	1.74	P=0.10 (insignificant)
Supine diastolic blood pressure	-22.56	+11.22	-12.11	+7.28	10.45	4.46	2.34	P<0.05>0.02 (significant)
Standing systolic blood pressure	-45.44	±20.37	-30.33	±10.05	15.11	7.57	2.0	p>0.05 (insignificant)
Standing Diastolic blood pressure	-20.33	±10.21	-8.56	±5.36	11.77	3.84	3.07	P<0.01>0.001 Very significant
Heart Rate in Hypertension patients	-20.00	±4.42	-18.00	±6.86	2.00	2.72	0.74	P>0.10 (insignificant)
Triglycerides	-27.5	± 33.43	+36.67	± 36.14	64.17	20.10	3.19	P<0.01>0.001 Very Significant
Cholesterol	-18.83	± 25.69	± 15.67	± 32.56	34.50	16.93	2.04	p>0.05 (insignificant)
HDL	+6.17	± 4.83	-3.17	+ 3.01	-9.34	2.32	-4.03	p>0.10 (insignificant)
VLDL	-7.50	± 13.40	0	± 10.66	+7.50	6.99	1.07	p>0.10 (insignificant)
LDL	-26.67	+19.90	-1.17	±18.87	+25.50	11.06	2.31	P<0.05>0.02 (significant)
Heart rate in Myocardial infarction patients	-5.00	+4.73	-9.33	± 13.76	4.33	5.94	0.73	p>0.10 (insignificant)
P R Interval	+0.003	± 0.019		+0.022	-0.03	0.012	-2.50	p>0.10 (Insignificant)
Heart Rate in E.C.G	+6.33	± 5.13	-11.17	± 15.85	-4.84	6.80	-0.71	p>0.10 (insignificant)

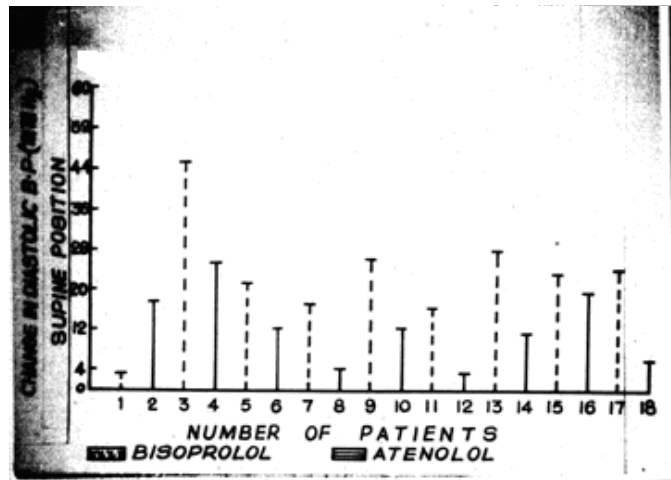
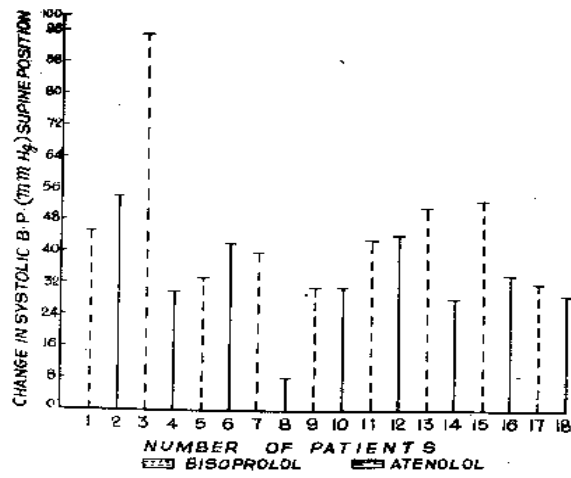
Table 2: Bisoprolol In Myocardial Infarction

Sl.No.	Age	Amount of Ischemia	Other Associated Disease	Response
1.	62	Inf. Apical QMI	Nil	Symptoms reduced after 2 hrs.
2.	43	Inf. Wall Ischemia	Nil	Symptoms reduced after 6 hrs.
3.	50	Antero Septal QMIc old apicolateral non QMI	Nil	Symptoms reduced after 12 Hrs.
4.	60	Ant Wall ischemia	Nil	Symptoms reduced after 12 Hrs.
5.	52	Ischemia	Nil	Drug is discontinued due to side effects (tingling and numbness of head)
6.	50	Apical and subepithelial injury	Diabetes+HTN	Symptoms reduced after 12 Hrs.
7	50	Apical and apicolateral ischemia	Nil	Symptoms reduced after 24 hrs.

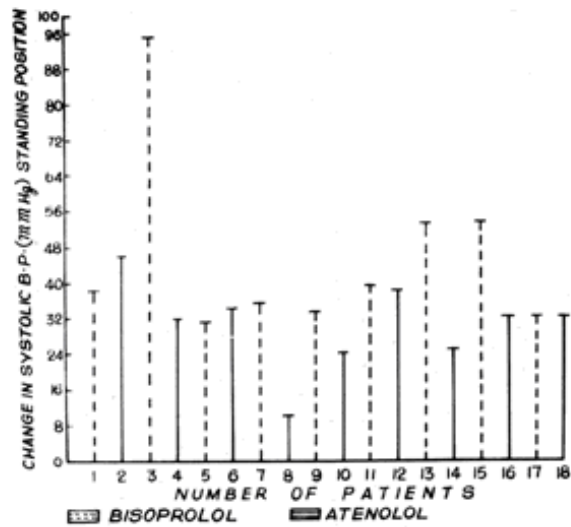
Table 3 .Atenolol I N Myocardial Infarction:

Sl.No.	Age	Amount of Ischemia	Other Associated Disease	Response
1.	40	Ischemia	Nil	Symptoms reduced after 6 hrs.
2.	70	Old Inf. QMI with apical non QMI	Nil	Symptoms reduced after 12 hrs.
3.	28	Ant wall sub epithelial injury	Nil	Symptoms reduced after 24 Hrs.
4.	60	Old antero inf. QMI	Nil	Symptoms reduced after 24 Hrs.
5.	60	Occasional PVC Old Inf QMI	HTN	Symptoms reduced after 24 Hrs.
6.	40	High lateral wall ischemia	Nil	Symptoms reduced after 48 Hrs.
7	50	Inf. QMI	Nil	Symptoms reduced after 12 Hrs, but 6 days after therapy he again developed ischemic changes. So, the drug is discontinued.

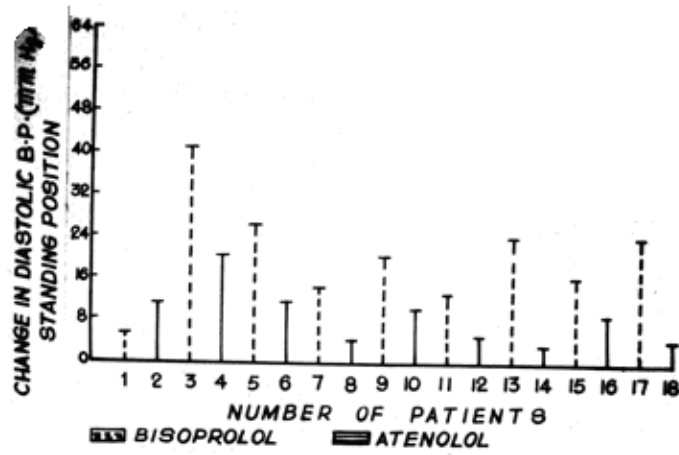
Graph-1



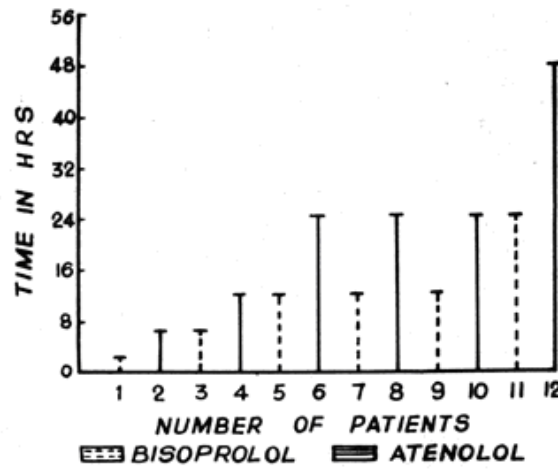
Graph-2



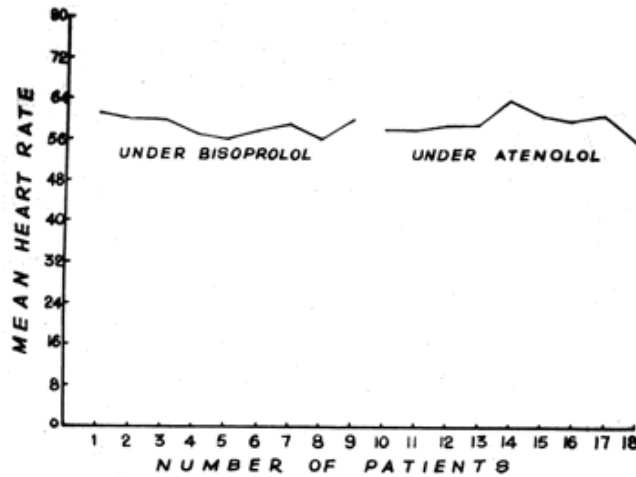
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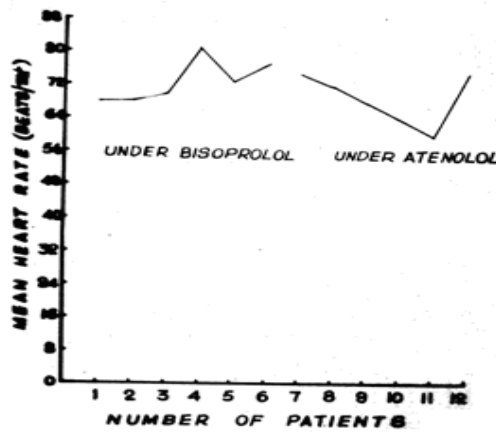
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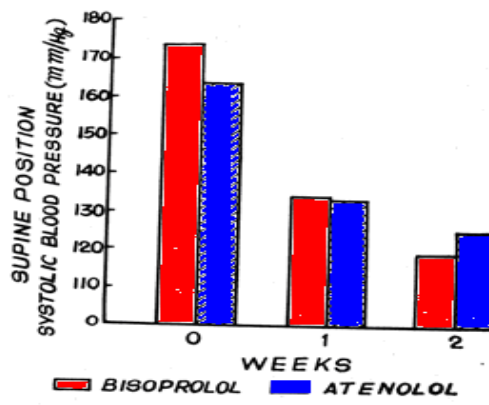
Graph-5



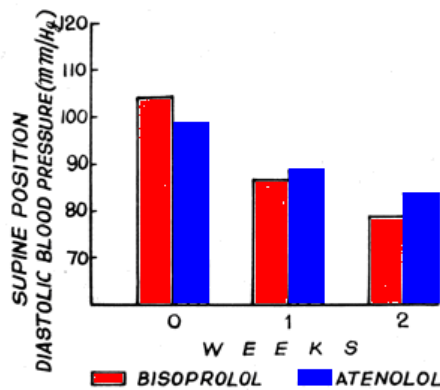
Graph-6



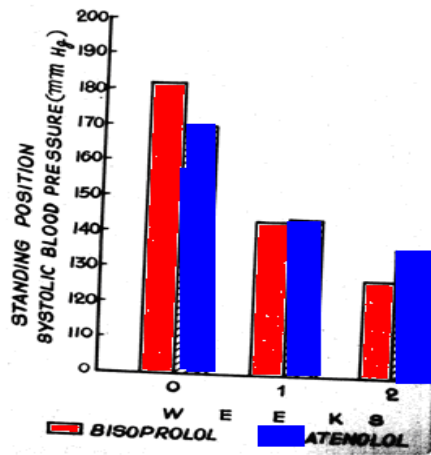
Graph-7



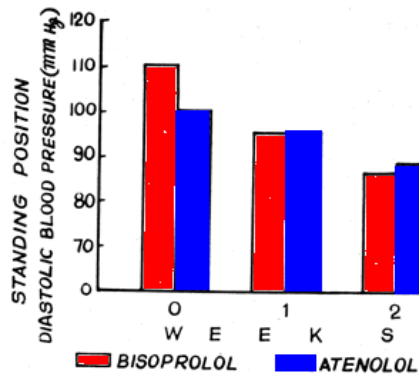
Graph-8. Mean Blood pressure readings before and after treatment with bisoprolol or Atenolol



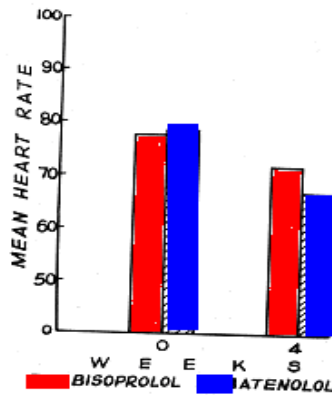
Graph-9. Mean Diastolic blood pressure in supine position before and after treatment with Bisoprolol or Atenolol



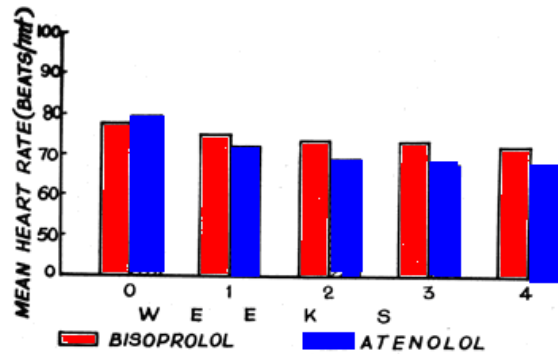
Graph-10. Mean Systolic Blood pressure in Standing Position Before and after treatment with Bisoprolol or Atenolol



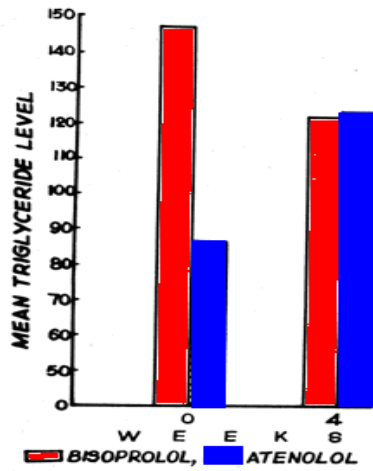
Graph-11



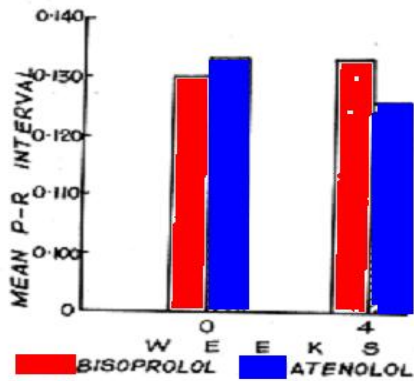
Graph-12



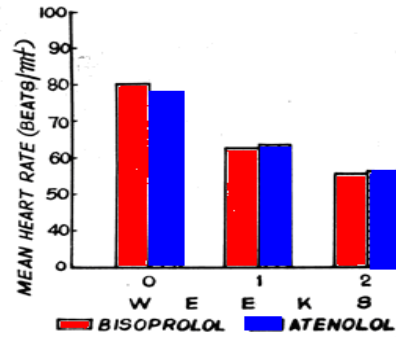
Graph 13



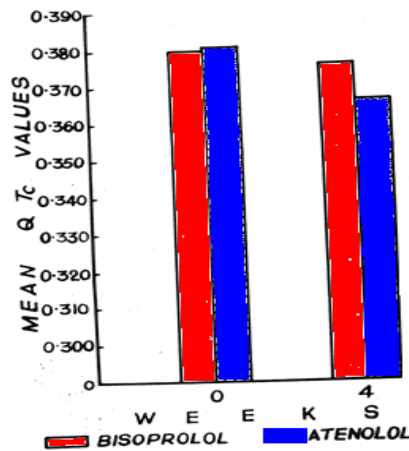
Graph-14



Graph 15 .Mean P.R Interval in myocardial infarction patients seen before and after treatment



Graph-16 Mean Heart Rates in myocardial infarction patients seen before and after treatment



Graph 17 .Mean QTC values in Myocardial Infarction Patients seen before and after treatment

VI. Summary And Conclusion

The present study is double blind study of bisoprolol and atenolol in myocardial infarction Bisoprolol had a consistently greater antihypertensive effect than Atenolol. The difference in antihypertensive effect between Atenolol and Bisoprolol were statistically very significant for diastolic blood pressure ($p < 0.05 > 0.02$). In supine as well as standing position. ($p < 0.01 > 0.001$).

In myocardial infarction Bisoprolol worked more quickly than Atenolol. It reduced the symptoms from 2hrs to 24 hrs. Atenolol reduced it from 6 hrs to 48 hrs. Both drugs reduced the QTC values but the difference between the two was not statistically significant ($p < 0.10$).

6.1Lipid Profile Values

Bisoprolol significantly decreased the triglyceride level ($p < 0.01 > 0.001$) as well as LDL levels ($p < 0.05 > 0.02$). The difference between the two drugs in other parameters was not statistically significant.

6.2Adverse Effects:

Adverse effects were same for the two drugs. But the symptoms disappeared early in the case of bisoprolol than Atenolol.

So, Bisoprolol which is a new highly beta 1 selective beta adrenoceptor antagonist did well both in Hypertension and Myocardial infarction when compared to Atenolol. Because of non availability of drug and its high cost do not

make use possible to recruit large number of patients. So further studies using large number of patients were necessary to confirm the results.

Each tablet of Bisoprolol cost is Rs 8 If the cost was reduced it is very much beneficial to the people

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